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Discontinuous conduction in mouse bundle branches is caused by bundle-branch architecture.

van Veen TA, van Rijen HV, van Kempen MJ, Miguerol L, Opthof T, Gros D, Vos MA, Jongsma HJ, de Bakker JM.

Department of Medical Physiology, University Medical Center Utrecht, Utrecht, The Netherlands. A.A.B.vanVeen@med.uu.nl

BACKGROUND: Recordings of the electrical activity of mouse bundle branches (BBs) suggest reduced conduction velocity (CV) in the midseptal compared with the proximal part of the BB. The present study was performed to elucidate the mechanism responsible for this slowing of conduction. METHODS AND RESULTS: Hearts of 16 mice were isolated and Langendorff perfused. After the right and left ventricular free walls were removed, the extracellular activity of the BB was mapped with a 247-point electrode. Premature stimulation was used to estimate CV restitution in the BBs. Expression/distribution of connexin40 (Cx40), Cx43, and Cx45 was determined. Morphology of the conduction system was assessed by whole-mount acetylcholine esterase staining and in Cx40(+/KI-GFP) hearts. Effective CV in the midseptal part of the left and right BBs was reduced by 50% compared with the proximal BB. CV restitution in the proximal and midseptal parts of the BBs was similar. Myocytes labeled positive for Cx40 and Cx45 in the entire BB. Cx43 colocalized with Cx40 and Cx45 only in the very distal BB. Subcellular distribution of gap junctions differed between proximal and distal BBs. Geometry of the midseptal and distal BBs revealed on both sides a profuse network of interlacing fibers, whereas the proximal BB consisted of a single (right BB) or multiple (left BB) parallel fibers. CONCLUSIONS: Comparison of connexin expression/distribution, geometry of the BBs, and CV characteristics suggests that increased path length for activation resulting from BB geometry is responsible for the apparently reduced CV in the midseptal BB of the mouse heart.

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